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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/022,799	12/20/2001	Beuford Arlie Bogue	24720	4794

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EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 12/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/022,799	BOGUE, BEUFORD ARLIE	
	Examiner	Art Unit	
	Lakshmi S Channavajjala	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Receipt of response filed 9-24-03 is acknowledged.

Claim Rejections - 35 USC § 103

Claims 1-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,197,349 to Westesen et al ('349).

'349 teach drug delivery systems comprising particles made of super cooled melt of a poorly water-soluble substance and a stabilizing agent, where the mean particle size is between 30 and 500 nm (abstract, col.7, lines 25-54). The particles of '349 exist primarily in amorphous phase (col.1). '349 teach that solubilization of otherwise insoluble drugs cab be achieved by reducing particle size or improving wettability of particles by hydrophilization or by reducing crystallinity of the substance (col. 2, lines 13-60). In particular, "349 teach that the addition of surfactants as wetting agents increase the wettability of particles, which can be further increased if the drug is not in crystalline form but in amorphous form, because the latter exhibits high solubility and fast dissolution that their crystal forms (col. 5, lines 30-56). For the process of preparing the microparticles, '349 teaches preparing a dispersion of water-insoluble drug with a stabilizer (such as surfactants), which is then emulsified above the melting point of the substance or mixture of substances (col. 10, lines 1-26) and then subject to vortexing (which reads on shear force) resulting in fine particle preparation. Further, '349 teach that ionic and nonionic surfactants stabilize the particles formed in the above process and suggest several surfactants (col.12) for stabilization. '349 teach choosing a proper emulsifier prevents the de-crystallization of the substances. '349 teach several drugs or therapeutics (col. 13) and teach the final particle size of below 150 nm (col.14). '349 does not state whether the drug and surfactant are

chemically bonded. '349 also fails to state if a matrix is formed between drug and substance and also if the substance is free flowable as in claim 18. However, '349 teaches the same steps of mixing the surfactants with the drugs that are poorly soluble and emulsified above melting point of the mixture, which is accomplished only by heating and accordingly, absent showing evidence to the contrary, a matrix is formed in the process. Further, '349 teach vortexing or vigorous shaking for forming the nano or microparticles, which are "non-crystalline or amorphous". Thus, the process reads on the instant shear force and accordingly, results in a free flowing substance. Therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to mix a drug that is poorly soluble with a stabilizer such as surfactant that increases the wettability of the drug and prepare particles by the process of '349 because the process taught by '349 results in amorphous and non-crystalline particles of lower than 150 nm, which is also the particle size range claimed and '349 teach that such amorphous particles (called super cooled particles) increase the wettability of the otherwise insoluble substances. Therefore, one of an ordinary skill in the art would expect an improved delivery with increased bioavailability (col.14). '349 do not teach the claimed additives, excipients, carriers etc. However, incorporating the above in drug delivery compositions is routine and accordingly would have been obvious for a skilled artisan to achieve the art-recognized effect.

Response to Arguments

Applicant's arguments filed 9-24-03 have been fully considered but they are not persuasive.

Applicants argue that '349 does not teach or suggest applicants' inventive subject matter as whole and that there is no suggestion that leads one of an ordinary skill in the art to modify the reference as defined in the claims. Applicants argue that the '349 fail to teach the inventive step of instant claims i.e., cooling under high shear force, which applicants urge is essential for improved dissolution of the drug and in the absence of which crystals grow on the exterior of the surfactant (page 6 of response). Applicants argue that the step of vortexing taught by '349 pertains to the emulsification and/or predispersion and that the product obtained by '349 is not the same as the instant product because the lack of the cooling a mixture under high shear. Further, applicants argue that one of an ordinary skill in the art would not be lead to attempt cooling the mixture under high shear, as the patent does not recognize the need. Finally, applicants argue that '349 patent teaches items that are not concerned with the present claims such as wettability.

Applicants' arguments have been fully considered but not found persuasive because instant claim 1 is directed to micro or nano particulate drug composition comprising a drug and a surfactant, which is taught by '349. The limitations "form a surfactant-drug matrix at a temperature above matrix's melting temperature" and "form a non-crystalline or micro- or nano-sized crystals ...while being cooled to room temperature under shearing force" denote future intended use and not positive steps. Further, instant shearing force is a relative term and applicants have not described the actual force or range of forces. The examples of instant application state that drug and surfactant are vigorously shaken and do not mention the force used. The method of '349 differ from that of the instant claims only in the step of cooling, as can be seen from the examples of '349 where the final mixture is cooled to room temperature.

However, '349 also desire a particulate composition (having particle size in the same range as that claimed) and teaches that improved bioavailability of the drug depends on the particle size and in particular states that the absence of crystallinity or rather an amorphous state exhibits higher or faster dissolution than their crystal forms since dissolution of amorphous substance does not require a lattice energy (col. 5). Instant application also describes the same theory behind the instant invention. Thus, both instant and '349 desire a particulate drug, which is amorphous for improved dissolution. Thus, when the prior art achieves the same end product, the process by which the product is prepared does not carry patentable weight. Furthermore, instant claim 1 recites drug and surfactant form a non-crystalline substance or a micro or nanoparticle sized crystals, suggesting that instant method does not necessarily result in amorphous particles, while '349 teach particulate material that is amorphous, which has better dissolution characteristics. With respect to applicants' arguments regarding the improved dissolution, none of the claims recite the limitation. Accordingly, employing the step of shaking (with varying force as desired) with an expectation of obtaining particulate composition containing drug and a stabilizing surfactant exhibiting good dissolution and bioavailability would have been obvious from the teachings of '349.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S Channavajjala whose telephone number is 703-308-2438. The examiner can normally be reached on 7.30 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-7924 for regular communications and 703-308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Lakshmi S Channavajjala
Examiner
Art Unit 1615
December 23, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600